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Chimeric Fc receptors identify functional domains of the murine high affinity receptor for IgG.

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Chimeric Fc gamma R have been generated between the mouse high affinity receptor for IgG (Fc gamma RI) and the low affinity receptor for IgG (Fc gamma RII) by exchanging the first two domains of the three-domain extracellular structure of Fc gamma RI with the homologous two-domain extracellular structure of Fc gamma RII. Studies of the affinity and specificity of binding of mouse Ig classes to these receptors defined functional regions of Fc gamma RI and showed some surprising results. After removal of the third extracellular domain of Fc gamma RI, the remaining two domains (domains 1 and 2) retained the capacity to bind Ig in the form of immune complexes, however, they bound monomeric IgG2a with a reduced affinity. Surprisingly, these two domains in the absence of the third domain bound not only IgG2a but also IgG1 and IgG2b, i.e., the third domain of Fc gamma RI suppresses the intrinsic capacity of the first two domains to act as a low affinity Fc gamma RII-like molecule. Linking the third extracellular domain of Fc gamma RI to the two extracellular domains of Fc gamma RII resulted in a receptor that retained the specificity and affinity of Fc gamma RII. Thus, the removal of domain 3 from Fc gamma RI resulted in the conversion of Fc gamma RI to an "Fc gamma RII-like" receptor. These findings indicate that domains 1 and 2 of Fc gamma RI form an Ig-binding motif, and although domain 3 is not essential for Fc binding by Fc gamma RI, it plays a crucial role in determining the specific high affinity interaction of Fc gamma RI with IgG2a.

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